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NEUROHUMORAL CONTROL MECHANISMS IN THE REGULATION OF CARDIOVASC--ETC(U)
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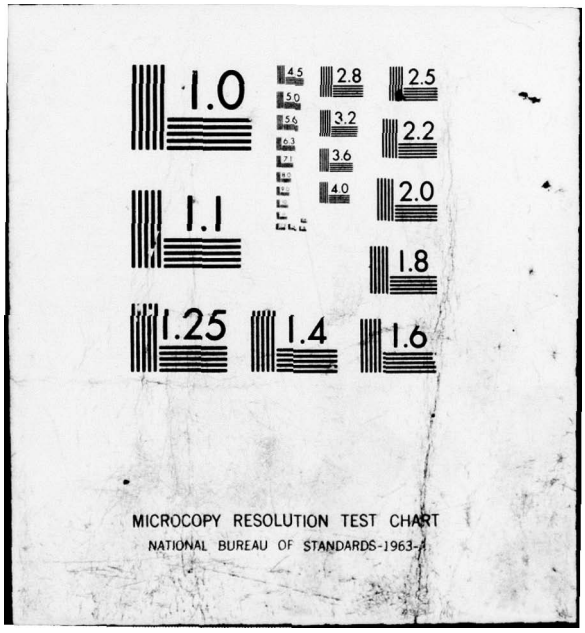
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20. Abstract

Changes in cardiac output and peripheral resistance, and changes in the venous tone following bleeding and transfusion, and their correlation with the cardiac and sino-aortic receptor drive were studied.

Additional studies were made of cardio-acceleratory sympathetic afferent pathways, physiology of arterio-venous (A-V) shunts, including the mechanism underlying cardio-vascular adjustment in A-V shunts, and cardio-vascular receptors discharge in A-V shunts. Also studied were the response of vagal afferents in shock and fainting, vagal and/or non-vagal pathways concerned with sympathetic outflow to the spleen and kidneys, and mechanisms of natriuresis produced by instillation of sodium into the third ventricle.

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NEUROHUMORAL CONTROL MECHANISMS IN THE REGULATION OF CARDIOVASCULAR FUNCTION AND FLUID AND ELECTROLYTE BALANCE

(October 1, 1971 to September 30, 1976)

P.D.Gupta
Vallabhbhai Patel Chest Institute
University of Delhi
Delhi - 110 007
INDIA

FDG/Physiol

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NEUROHUMORAL CONTROL MECHANISMS IN THE REGULATION OF CARDIOVASCULAR FUNCTION AND FLUID AND ELECTROLYTE BALANCE

(Final Scientific Report under Grant No. AFOSR 71 2149)

I. SPINAL AUTONOMIC AFFERENTS IN ELICITATION OF TACHYCARDIA IN VOLUME INFUSION IN THE DOG.

Investigator: P.D.Gupta, M.D.

Bainbridge reported in 1915 that an intravenous infusion in aesthetised dogs resulted in an increase in heart rate. This response is considered a reflex with the efferent pathway in both vagus and sympathetic nerves. However, inadequate information is available concerning the afferent pathways which contribute to the tachycardia response evoked by infusion. This study was undertaken with a view to define the afferent pathways which are activated by volume infusion.

Experiments were performed on 27 animals. Intravenous infusion of blood (36 ml/kg body wt) elicited tachycardia in artificially ventilated anesthetised dogs with intact autonomic innervation and in dogs with cardiac beta-receptor blockade. In contrast, infusion elicited bradycardia in dogs with section of the spinal cord at C_6-C_7, and in dogs with combined spinal section and cardiac beta-receptor blockade. The control heart rate was 110 beats/min in all the animals. The presence of infusion-induced tachycardia in dogs with beta-receptor blockade, i.e., dogs in which cardiac sympathetic efferents were blocked, and its absence in dogs with combined spinal section and beta-receptor blockade,

i.e., dogs in which spinal autonomic afferents plus cardiac sympathetic efferents were blocked, may be the result of an additional interruption of spinal autonomic afferents by spinal section. It is concluded that tachycardia elicited by infusion may be partly due to a reflex with its afferent pathway in the spinal cord and its efferent pathway in the vagus nerves.

This work was published in the Am. J. Physiol. 229: 303-308, 1975.

II. AUTONOMIC AFFERENTS AT T-1 IN ELICITATION OF VOLUME-INDUCED TACHYCARDIA IN THE DOG.

Investigator: P.D.Gupta and M.Singh

In the study cited above (Am. J. Physiol. 229: 303-308, 1975), it was shown that volume infusion activated a cardioacceleratory reflex with its afferent pathway in the spinal cord, and its efferent pathway in the vagus nerves. Except suggesting that the afferent pathway of this reflex could make its entry caudal to C-7 spinal roots, the above study did not indicate the actual segments at which it enters the spinal cord. Accordingly, 112 experiments were performed with a view to localise the segments at which the volume-activated afferents enter the spinal cord. Intravenous infusion of blood elicited tachycardia in anesthetised dogs with beta-receptor blockade (dogs with vagal efferents intact but cardiac sympathetic efferents blocked), and bradycardia in dogs with combined beta-receptor blockade and rhizotomy at T-1 (dogs with vagal efferents intact but cardiac sympathetic efferents plus autonomic afferents at T-1 blocked)

This suggests that tachycardia elicited by volume infusion may be partly due to a reflex with its afferent pathway at the T-1 segment of the spinal cord, and its efferent pathway in the vagi. Moreover, infusion evoked bradycardia in dogs with right-sided rhizotomy at T-1 which was not significantly different from the response elicited in dogs with bilateral rhizotomy at T-1. Additionally, the tachycardia response induced in dogs with ventral or dorsal rhizotomy at T-1 was significantly different from the bradycardia response elicited in dogs with both dorsal and ventral rhizotomy at T-1. These results suggest that the afferent pathway predominates on the right side, and its entry at T-1 may be via both dorsal and ventral roots. Also, in dogs with spinal section at T-1 (caudal to T-1 spinal roots) or T-7, or dogs with rhizotomy at individual segments at C-8, and T-2-to-7, infusion evoked heart rate response which was not significantly different from the response in control dogs. This indicates that afferents at these segments did not make a significant contribution to infusion-induced tachycardia.

This work was presented at the International Symposium on Cardiac Receptors, Leeds, England, September 16, 1976. A monograph is likely to be published based on the proceedings of the symposium. The reprints will be sent on receipt.

This work also has been accepted by the A. J. Physiol. for publication (1977, in press). The reprints will be sent on receipt.

III. A METHOD FOR LOCALIZING ATRIAL TYPE B RECEPTORS IN THE DOG.

Investigator: M.Fahim, Ph.D.

The effect of ectopic stimulation of atria (premature ventricular contraction) on the activity of atrial type B receptors has been studied in dogs.

In sixteen open-chest dogs, discharge from right or left atrial type B receptors (identified by their response to pulmonary artery occulusion) was recorded. Direct stimulation of either atrium produced an increase in the activity of the left atrial but a decrease in the right atrial receptors. The earlier during the ventricular systole that the premature ventricular contraction occurred the more marked was the effect.

In a separate series of fourteen closed chest experiments the right atrium was stimulated internally via the external jugular vein. The effects on the activity of the atrial type B receptors were similar to those observed during the open chest experiments.

It is concluded that in the dog, the technique of internal stimulation of the right atrium without opening the chest can be used to distinguish between the right and left atrial type B receptors.

This work has been accepted for publication in Clinical and Experimental Pharmacology and Physiology (Australia) (1977, in press). The reprints will be sent on receipt.

IV. EFFECT OF PROPRANOLOL ON THE RELATIONSHIP BETWEEN ATRIAL SYSTOLIC PRESSURE AND TYPE A ATRIAL RECEPTOR DISCHARGE IN CATS.

Investigator: P.S.Rao, M.D., and M.Fahim, Ph.D.

The response of type A atrial receptors to graded infusions of saline and large doses of propranolol were examined in anesthetized cats. Infusion of saline raised the mean atrial pressure, but usually the amplitude of the atrial a wave was reduced. In general the receptor discharge was unaffected. Propranolol reduced the discharge from the control level when it was injected in doses not less than 4 mg/kg. Infusions of saline after propranolol resulted in an increase in the discharge and the increase was related to the amplitude and/or initial pressure of the a wave. In one case the discharge after propranolol was less than that when the atrium was widely slit open. It is concluded that at least part of the effect of the drug is due to a direct depression of the receptor rendering it less sensitive to the stretch provided by atrial contraction. The demonstration of a stimulus-response relationship between the a wave and the receptor discharge at low levels of activity suggests that under normal conditions the receptor operates on a plateau of maximum activity, thus making a response to small changes in stimulus strength obscure.

This work has been published in Archives Internationales de Pharmacodynamie et de Therapie (Belgium). 223: 43-53, 1976. The reprints will be sent on receipt.

V. RELATIVE DISTRIBUTION OF TYPES A AND B ATRIAL RECEPTORS IN DOGS, CATS, MONKEYS AND RABBITS.

Investigators: P.S.Rao, M.D., M.Fahim, Ph .D., B.N.Gupta, Ph.D.

The frequency distribution of different types of atrial receptors was as following:

Animals	No. of Animals	No. of atrial receptors A	B	Intermediate	A:B
Cats	14	35	61	11	1:1.8
Dogs	20	3	47	2	1:16
Monkeys	8	0	8	0	0:8
Rabbits	20	0	0	0	0:0

From this table it is clear that the relative distribution of the two main types of atrial receptors is different in different animals. Whether this difference in the frequency distribution of type A and B atrial receptors among various species also represents functional difference remains to be established.

This series was published in Experentia. 31: 1174-1175, 1975.

VI. FRACTIONATION OF TOTAL CORONARY BLOOD FLOW (TCF) INTO NUTRITIONAL (NCF) AND SHUNT FLOW (SF) IN CORONARY HYPERAEMIA AND ISCHEMIA INDUCED BY VARYING SYSTOLIC PRESSURES IN THE ISOLATED PERFUSED DOG HEART.

Investigators: A.Edalji Kumar, R.Kumar, M.Singh, H.S.Yadav, B.N.Chaudhuri, C.K.Gupta and P.D.Gupta

During elevation of systolic pressure, the increase in TCF is in excess of the oxygen need of myocardium. In an isolated perfused canine heart preparations, 5 hearts each were studied at

left ventricular systolic pressure of 50, 100 (Control), 150 and 200 mmHg. TCF was measured by rotameter (TCF Ro). Utilizing ^{86}Rb the TCF was determined by Fick principle (TCF Rb) and NCF by the clearance technique; SF was calculated as the difference of TCF Rb and NCF. TCF Rb was 40 ± 3, 67 ± 14, 133 ± 20 and 238 ± 38 ml/min/100 g at corresponding systolic pressures and was similar to TCF Ro (r = 0.98). SF constituted a higher fraction of TCF Rb (13, 28, 32 and 50%) at increasing pressures. Pressure-induced increase in MVO_2 (4.0, 5.2, 9.4 and 12.0 ml/min/100 g) was associated with decreasing coronary A-VO_2 differences of the same magnitude as the increase in SF; indicating that if the A-VO_2 had remained constant the increase in TCF Rb would have been similar to NCF. The predicted and measured NCF show significant correlation (r = 0.95). It is concluded that in pressure-induced hyperemia and ischemia SF constitutes a significant fraction of TCF at higher pressures. It is possible that in other hyperemic states the relative contribution of SF to TCF/upon the cause of /- depend hyperemia.

VII. MECHANISM OF NATRIURESIS PRODUCED BY INSTILLATION OF SODIUM INTO THE THIRD VENTRICLE.

Investigator: M.A.Kumar, M.D., Ph.D.

Hypertonic saline injected into the third ventricle of anesthetized dogs and monkeys failed to produce unequivocal natriuresis.

VIII. PRESSURE-VOLUME RELATIONSHIPS IN THE LEFT ATRIA OF ANESTHETIZED DOGS.

Investigator: M.Fahim, Ph.D, and K.S.Krishnamurthy, Ph.D.

Experiments were carried out on 7 dogs. Controlled volumes of saline were injected into the left atrium using a method by which the injections were triggered by the R wave of the normal EKG during the period of the V wave of the left atrial pressure waveform. The resulting change in the amplitude of the V wave was found to be linearly related to the injected volume. This linearity in the pressure-volume relationship of the atrium extended down to a volume of 1.0 ml.

IX. REGIONAL DISTRIBUTION OF CARDIAC OUTPUT AND MYOCARDIAL BLOOD FLOW IN INTACT CONSCIOUS DOGS: EFFECT OF SODIUM PENTOBARBITAL ANESTHESIA OF ONE AND FOUR HOURS DURATION.

Investigators: R.Kumar, M.D. and P.D.Gupta.

Experiments were performed on 21 dogs. The results indicate that anesthesia does not significantly alter the blood flow to heart, kidney, lung and spleen. However, a marked decrease in flow and increase in resistance is observed in the portal and musculocutaneous beds. The changes in regional resistances are most marked at the end of one hour, and at four hours the general trend is a return of these values towards the control.

X. NEURAL MECHANISM UNDERLYING TACHYCARDIA INDUCED BY OPENING AN ARTERIO-VENOUS SHUNT IN ANESTHETIZED DOG.

Investigator: P.D.Gupta and M.Singh

The work is in progress.